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EXAMINER
LOEB, BRONWEN

ART UNIT	PAPER NUMBER
2636	11

DATE MAILED: 10/19/2002

Please find below and or attached an Office communication concerning this application or proceeding.

Application No.	Applicant(s)	
09/811,842	LINK ET AL.	
Examiner	**Art Unit**	
Bronwen M. Loeb	1636	

Office Action Summary

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 March 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4 & 7* .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☒ Other: *See Continuation Sheet* .

Continuation of Attachment(s) 6). Other: Copy of Papers Originally Filed information.

09/811,842

The following papers have not been made part of the permanent records of the United States Patent and Trademark Office (Office) for this application (37 CFR 1.52(a)) because of damage from the United States Postal Service irradiation process:

Mailroom Stamp Date	Certificate of Mailing Date
24 January 2002	15 November 2001

The above-identified papers, however, were not so damaged as to preclude the USPTO from making a legible copy of such papers. Therefore, the Office has made a copy of these papers, substituted them for the originals in the file, and stamped that copy:

COPY OF PAPERS
ORIGINALLY FILED

If applicant wants to review the accuracy of the Office's copy of such papers, applicant may either inspect the application (37 CFR 1.14(d)) or may request a copy of the Office's records of such papers (*i.e.*, a copy of the copy made by the Office) from the Office of Public Records for the fee specified in 37 CFR 1.19(b)(4). Please do **not** call the Technology Center's Customer Service Center to inquiry about the completeness or accuracy of Office's copy of the above-identified papers, as the Technology Center's Customer Service Center will **not** be able to provide this service.

If applicant does not consider the Office's copy of such papers to be accurate, applicant must provide a copy of the above-identified papers (except for any U.S. or foreign patent documents submitted with the above-identified papers) with a statement that such copy is a complete and accurate copy of the originally submitted documents. If applicant provides such a copy of the above-identified papers and statement within **THREE MONTHS** of the mail date of this Office action, the Office will add the original mailroom date and use the copy provided by applicant as the permanent Office record of the above-identified papers in place of the copy made by the Office. Otherwise, the Office's copy will be used as the permanent Office record of the above-identified papers (*i.e.*, the Office will use the copy of the above-identified papers made by the Office for examination and all other purposes). This three-month period is not extendable.

Part of Paper No. 11

DETAILED ACTION

This action is in response to the amendment to the specification filed 19 July 2002.

Claims 1-52 are pending.

Priority

1. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. § (120 or 119(e)) as follows:

The second application (which is called a continuing application) must be an application for a patent for an invention which is also disclosed in the first application (the parent or provisional application); the disclosure of the invention in the parent application and in the continuing application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. §112. See *In re Ahlbrecht*, 168 USPQ 293 (CCPA 1971).

Upon review of the specification of the parent (or provisional) application and comparison with the specification of the present application, it is determined that the specification of parent (or provisional) applications 60/190,678 and 60/198,722 are not enabling for the use and preparation of the instantly claimed invention. The specifications of the parent (or provisional) application do not teach or suggest the sequence tag acquisition and reporting method, the serial anaylsis of viral integration method, the plasmids pGT5A, pGT5AH, pGT5Z, pGT7A, pGT7AH and pGT7Z or the

specific steps of the correlating step recited in for instance in claims 17-20. The specifications teach a method of determining a protein expression profile using a construct that encodes hrGFP that is expressed only when integrated into an active transcription site and some details about the construct. Since the sequence tag acquisition and reporting method, the serial analysis of viral integration method, the plasmids pGT5A, pGT5AH, pGT5Z, pGT7A, pGT7AH and pGT7Z or the specific steps of the correlating step recited in for instance in claims 17-20 are not disclosed in the parent (or provisional) applications and cannot be predicted from the teachings of the parent (or provisional) applications, the parent (or provisional) applications are not enabling for the instantly claimed invention. Thus, the requirements of the first paragraph of 35 U.S.C. §112 have not been met. Accordingly, claims 17-20 and 37-52 are assigned an effective filing date of 19 March 2001 and claims 1-6 and 21-36 are assigned an effective filing date of 20 March 2000.

Drawings

2. The drawings are objected to because:

In Fig. 16, the word "expression" is misspelled.

In Fig. 18A "vector" is misspelled in process step 2 and "fluorescence" is misspelled in process box 3.

In Fig. 18B, box 4 refers to "monoclonal kB diagnostics". Is "kB" a typographical error for "Ab"?

A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Specification

3. The disclosure is objected to because of the following informalities:

Figures 2, 4-8, 10, 13, 17 and 18 are multi-paneled figures but this is not reflected in the Brief Description of the Drawings on pp. 9-14. The specification should be amended to recite, for instance, "Figures 13A-D are ...." on p. 12, line 4. Also, the legend for Fig. 18A does not define the abbreviations "STARS" and "SAVI" used in the figure.

On p. 9, the seventh line from the bottom, there are abbreviations "STARS" and "SAVI" for which no definitions are provided. On p. 13, the seventh line from the bottom, there is an abbreviation "MK" for which no definition is provided.

On pp. 60-61, there are several paragraphs whose relevance to the invention is somewhat unclear. For instance, there are references to "carcinogenic effects...of viral genes", "site-specific HPV integration" and "integrated viral transforming genes".

Appropriate correction is required.

4. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code on p. 31. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Objections

5. Claims 1, 8, 21, 51 and 52 are objected to because of the following informalities:

Claim 1 recites "introducing to the genome" and "integration of said polynucleotide construct to an actively transcribing". In both instances, the grammar would be improved by changing "to" to "into".

Claim 8 recites the abbreviation "hrGFP". Abbreviations should be defined at their first recitation in the claim set.

Claim 21 recites "introducing to the genome" and "integration of said polynucleotide construct to an actively transcribing". In both instances, the grammar would be improved by changing "to" to "into". Also in the phrase "introducing to the genome", genome should be plural.

Claim 51 recites "introducing to the genome" and "integration of said polynucleotide construct to an actively transcribing". In both instances, the grammar would be improved by changing "to" to "into".

Claim 52 recites "introducing to the genome" and "integration of said polynucleotide construct to an actively transcribing". In both instances, the grammar would be improved by changing "to" to "into".

Appropriate correction is required.

6. Claims 41-44 are objected to under 37 CFR 1.75 as being a substantial duplicate of claims 17-20, respectively. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in

wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

7. Claim 52 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 20. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 45-50 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 45-50 are drawn to a specific plasmids, pGT5A, pGT5AH, pGT5Z, pGT7A, pGT7AH and pGT7Z, respectively. The specification does not provide a repeatable method for obtaining any of these plasmids and none of them appear to be a readily available material. Deposit of each of these plasmids would satisfy the enablement requirements of 35 U.S.C. §112.

A declaration by applicant, assignee, or applicant's agent identifying a deposit of biological material and averring the following may be sufficient to overcome an objection or rejection based on a lack of availability of biological material. See 37 CFR 1.801 through 1.809. Such a declaration:

1. Identifies declarant.

2. States that a deposit of the material has been made in a depository affording permanence of the deposit and ready accessibility thereto by the public if a patent is granted. The depository is to be identified by name and address.

3. States that the deposited material has been accorded a specific (recited) accession number.

4. States that all restrictions on the availability to the public of the material so deposited will be irrevocably removed upon the granting of the patent.

5. States that the material has been deposited under conditions that assure that access to the material will be available during the pendency of the patent application to one determined by the Commissioner to be entitled thereto under 37 C.F.R. 1.14 and 35 U.S.C. § 122.

6. States that the deposited material will be maintained with all the care necessary to keep it viable and uncontaminated for a period of at least five years after the most recent request for the furnishing of a sample of the deposited microorganism, and in any case, for a period of at least thirty (30) years after the date of deposit or for the enforceable life of the patent, whichever period is longer.

7. That he/she declares further that all statements made therein of his/her own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements were made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the instant patent application or any patent issuing thereon.

Alternatively, it may be averred that deposited material has been accepted for deposit under the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure (e.g., see 961 OG 21, 1977) and that all restrictions on the availability to the public of the material so deposited will be irrevocably removed upon the granting of a patent.

Additionally, the deposit must be referred to in the body of the specification and be identified by deposit (accession) number, date of deposit, name and address of the depository, and the complete taxonomic description.

10. The following is a quotation of the second paragraph of 35 U.S.C. §112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 4, 5, 7, 8, 16-20, 24, 25, 27, 28 and 36-44 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 is vague and indefinite in reciting improper Markush group language. This rejection would be overcome by amending the claim to reciting "...adenovirus and [~~of~~] adeno-associated virus".

Claim 5 is vague and indefinite in reciting "The vector of claim 4..." because claim 4 is drawn to a method not a vector. This rejection would be overcome by amending the claim to recite "The method of claim 4 wherein said vector ...".

Claim 7 is vague and indefinite in reciting "The marker of claim 6..." because claim 6 is drawn to a method not a marker. This rejection would be overcome by

amending the claim to recite "The method of claim 6 wherein said assay marker peptide is green fluorescent protein".

Claim 16 is vague and indefinite in reciting "said reference is a colon cancer cell" because it depends on claim 15 which recites the "reference cell is a normal cell". This rejection would be overcome by amending the claim to recite "said test cell is a colon cancer cell and said reference cell is a colon cell".

Claim 17 recites the limitation "said separated cell" in line 3. There is insufficient antecedent basis for this limitation in the claim. This rejection would be overcome by amending the claim to recite "said sorted cell".

Claim 17 is vague and indefinite in reciting "said cleaved region" in line 6. It is unclear to what this refers exactly. If the nucleic acid is cleaved, that must result in at least two pieces of nucleic acid (assuming the nucleic acid is not circular). To which of these resultant nucleic acid pieces does this phrase refer?

Claim 17 is vague and indefinite in reciting "cleaving said nucleic acid material so that the region of integration...is separated". From what is the region separated?

Claim 18 is vague and indefinite in reciting "cleaved in a region contiguous to the inserted polynucleotide". The specification does not define what the phrase "a region contiguous to" means precisely and there is not an art-recognized definition for this phrase.

Claim 19 is vague and indefinite as it is unclear what the "fixed distance" is in the recitation "cleaving said nucleic acid at a site that is a fixed distance from said

integrated polynucleotide". If the site of integration is unknown and the flanking sequence is unknown, what "fixes" the distance of the site of cleavage?

Claim 20 is vague and indefinite in reciting "said cleaved nucleic acid" in line 2. It is unclear to what this refers exactly. If the nucleic acid is cleaved, that must result in at least two pieces of nucleic acid (assuming a non-circular nucleic acid). To which of these resultant nucleic acids does this phrase refer?

Claim 24 is vague and indefinite in reciting improper Markush group language. This rejection would be overcome by amending the claim to reciting "...adenovirus and [~~or~~] adeno-associated virus".

Claim 25 is vague and indefinite in reciting "The vector of claim 4..." because claim 4 is drawn to a method not a vector. This rejection would be overcome by amending the claim to recite "The method of claim 4 wherein said vector ...".

Claim 27 is vague and indefinite in reciting "The marker of claim 6..." because claim 6 is drawn to a method not a marker. This rejection would be overcome by amending the claim to recite "The method of claim 6 wherein said assay marker peptide is green fluorescent protein".

Claim 36 is vague and indefinite in reciting "said reference cell population is a colon cancer cell" because it depends on claim 35 which recites the "reference cell population is a normal cell population". This rejection would be overcome by amending the claim to recite "said test cell population is a colon cancer cell population and said reference cell population is a colon cell population".

Claim 37 recites the limitation "said separated cell" in line 3. There is insufficient antecedent basis for this limitation in the claim. This rejection would be overcome by amending the claim to recite "said sorted cell".

Claim 37 is vague and indefinite in reciting "said cleaved region" in line 6. It is unclear to what this refers exactly. If the nucleic acid is cleaved, that must result in at least two pieces of nucleic acid (assuming the nucleic acid is not circular). To which of these resultant nucleic acid pieces does this phrase refer?

Claim 37 is vague and indefinite in reciting "cleaving said nucleic acid material so that the region of integration...is separated". From what is the region separated?

Claim 38 is vague and indefinite in reciting "cleaved in a region contiguous to the inserted polynucleotide". The specification does not define what the phrase "a region contiguous to" means precisely and there is not an art-recognized definition for this phrase.

Claim 39 is vague and indefinite as it is unclear what the "fixed distance" is in the recitation "cleaving said nucleic acid at a site that is a fixed distance from said integrated polynucleotide". If the site of integration is unknown and the flanking sequence is unknown, what "fixes" the distance of the site of cleavage?

Claim 40 is vague and indefinite in reciting "said cleaved nucleic acid" in line 2. It is unclear to what this refers exactly. If the nucleic acid is cleaved, that must result in at least two pieces of nucleic acid (assuming a non-circular nucleic acid). To which of these resultant nucleic acids does this phrase refer?

Claim 41 recites the limitation "said separated cell" in line 3. There is insufficient antecedent basis for this limitation in the claim. This rejection would be overcome by amending the claim to recite "said sorted cell".

Claim 41 is vague and indefinite in reciting "said cleaved region" in line 6. It is unclear to what this refers exactly. If the nucleic acid is cleaved, that must result in at least two pieces of nucleic acid (assuming the nucleic acid is not circular). To which of these resultant nucleic acid pieces does this phrase refer?

Claim 41 is vague and indefinite in reciting "cleaving said nucleic acid material so that the region of integration...is separated". From what is the region separated?

Claim 42 is vague and indefinite in reciting "cleaved in a region contiguous to the inserted polynucleotide". The specification does not define what the phrase "a region contiguous to" means precisely and there is not an art-recognized definition for this phrase.

Claim 43 is vague and indefinite as it is unclear what the "fixed distance" is in the recitation "cleaving said nucleic acid at a site that is a fixed distance from said integrated polynucleotide". If the site of integration is unknown and the flanking sequence is unknown, what "fixes" the distance of the site of cleavage?

Claim 44 is vague and indefinite in reciting "said cleaved nucleic acid" in line 2. It is unclear to what this refers exactly. If the nucleic acid is cleaved, that must result in at least two pieces of nucleic acid (assuming a non-circular nucleic acid). To which of these resultant nucleic acids does this phrase refer?

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. §102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

13. Claims 5, 7, 25 and 27 have been examined assuming they are drawn to methods (see rejections above).

14. Claims 1-5, 9, 17-19, 21-25, 29, 37-39, 41-43 and 51 are rejected under 35 U.S.C. §102(b) as being anticipated by Ruley et al (USP 5,364,783; cited in IDS, Paper #7).

Ruley et al teach a method of promoter trapping using a nucleic acid construct which encodes a polypeptide that can only be expressed when integrated into actively transcribed chromosomal loci. The construct comprises a promoterless protein coding sequence encoding at least one polypeptide, such as luciferase or beta-galactosidase, and a translational stop sequence. The construct is a retroviral one. The cells comprising the integrated vector are selected by sorting based on fluorescence (FACS) or by panning (a mechanical method). The integrated loci which are identified in the method are subjected to molecular analysis which includes isolating nucleic acid from a

cell comprising an integrated construct, cleaving the nucleic acid to isolate the integrated construct along with unknown sequence, ligating the cleaved nucleic acids to form an amplicon, amplifying it, sequencing it and comparing the sequence to known sequences in Genbank and EMBL to identify the sequence. The method may be used generally to identify and study genes during a process such as development which are identified by observing expression before and after the development (ie. a reference cell compared to a test cell). Identifying a series of genes by assessing expression of the selectable marker protein whose expression changes as a result of development thus establishes a protein expression profile. See entire document, especially Figure 8, col. 3, line 25- col. 4, line 56, col. 6, line 3- col. 6, line 57, col. 7, line 59-col. 8, line 64, col. 15, line 43-col. 16, line 48 and col. 17, line 32-36.

15. Claims 1-7, 9-15, 21-27 and 29-35 are rejected under 35 U.S.C. §102(e) as being anticipated by Baetscher et al (USP 5,922,601; cited in IDS, Paper #4).

Baetscher et al teach a method of gene trapping using a nucleic acid construct which encodes a polypeptide that can only be expressed when integrated into actively transcribed chromosomal loci. The construct comprises a promoterless protein coding sequence encoding at least one polypeptide providing positive and negative selection (selectable markers), a functional splice acceptor, a translational stop sequence and an internal ribosome entry site. The construct is preferably a viral vector, such as adenovirus and adeno-associated virus, and preferably is a retroviral vector. An example of a selectable marker includes green fluorescent protein, which allows sorting of the cells by fluorescent activated cell sorting. Another example is luciferase, allowing

sorting based on chemiluminescence. Other selectable markers include drug-resistance markers. The integrated loci which are identified in the method are subjected to molecular analysis to determine the chromosomal loci of the trap integration. The method may be used generally to identify genes whose activity is regulated upon a cellular transition event which are identified by observing expression before and after the transition event (ie. a reference cell compared to a test cell). Such cellular transition events include genes regulated during tissue differentiation, genes involved in oncogenesis, genes associated with tumorigenesis or identifying genes regulated upon tumor formation. Identifying a series of genes by assessing expression of the selectable marker protein (eg. GFP) and whose expression changes, for example, during tumorigenesis thus establishes a protein expression profile. See entire document, especially col. 4, line 43-col. 6, line 17, col. 7, line 43-col. 8, line 26, col. 8, lines 44-57, col. 10, lines 12-29 and 34-67, col. 13, lines 52-56 and col. 15, line 27-col. 16, line 37.

16. Claims 1-7, 9-14, 21-27 and 29-34 are rejected under 35 U.S.C. §102(e) as being anticipated by Whitney et al (US 2002/0025940 A1).

Whitney et al teach a method of gene trapping using a nucleic acid construct which encodes a polypeptide that is expressed when integrated into actively transcribed chromosomal loci. The construct comprises a promoterless protein coding sequence encoding a reporter gene, such as beta-lactamase, luciferase or GFP, a functional splice acceptor, a poly-adenylation sequence and an internal ribosome entry site. The construct may further comprise a positive selection marker, such as an antiobiotic

resistance factor. The construct may be a viral vector including retroviruses, adenoviruses, adeno-associated viruses and is preferably a retroviral vector. Cells may be sorted using FACS or chemiluminescence. The integrated loci that are identified in the method are subjected to molecular analysis (sequencing and comparison to known sequences using BLAST search techniques) to determine the chromosomal loci of the trap integration. The method may be used generally to identify genes which are directly or indirectly associated with a defined biological process or whose activity is altered as a result of an event, such as activation of a particular cell type (eg. PHA activation of T cells), which are identified by observing expression before and after the transition event (ie. a reference cell compared to a test cell). Identifying a series of genes by assessing expression of the selectable marker protein (e.g. GFP) and whose expression changes, for example, during cell activation or differentiation, thus establishes a protein expression profile. See entire document, especially paragraphs 0049-0138, 0146, 0162-0189, 0195-0200, 0225, Examples 7, 5 and 12 and claim 115.

Claim Rejections - 35 USC § 103

17. The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

18. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. §103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

19. Claims 1-15 and 21-35 are rejected under 35 U.S.C. §103(a) as being unpatentable over Baetscher et al in view of Li et al (USP 6,130,313).

Baetscher et al is applied as above to claims 1-7, 9-15, 21-27 and 29-35. Baetscher et al do not teach the use of a humanized green fluorescence protein (GFP) in their method.

At the time the invention was filed, it would have been obvious to one of ordinary skill in the art to employ a humanized GFP in the method of gene trapping taught by Baetscher et al. One of ordinary skill in the art would have been motivated to do so because such a humanized GFP has increased synthesis in mammalian cells, a feature which is advantageous for increasing the signal-to-noise ration when the method relies on fluorescence for detection and sorting. See for instance col. 1, lines 38-45 in Li et al.

20. Claims 1-7, 9-16, 21-27 and 29-36 are rejected under 35 U.S.C. §103(a) as being unpatentable over Baetscher et al in view of Vogelstein et al (WO 98/53319; cited in IDS, Paper #7).

Baetscher et al is applied as above to claims 1-7, 9-15, 21-27 and 29-35. Baetscher et al does not teach using their method to develop profiles of colon cancer cells.

At the time the invention was filed, it would have been obvious to one of ordinary skill in the art to apply the method of Baetscher et al to a colon cancer cell. One of ordinary skill in the art would have been motivated to do so because determining expression profiles in colon cancers is commonly performed (see for instance Vogelstein et al Table 1 and p. 96, Example 2).

21. Claims 1-14 and 21-34 are rejected under 35 U.S.C. §103(a) as being unpatentable over Whitney et al in view of Li et al (USP 6,130,313).

Whitney et al is applied as above to claims 1-7, 9-14, 21-27 and 29-34. Whitney et al do not teach the use of a humanized green fluorescence protein (GFP) in their method.

At the time the invention was filed, it would have been obvious to one of ordinary skill in the art to employ a humanized GFP in the method of gene trapping taught by Whitney et al. One of ordinary skill in the art would have been motivated to do so because such a humanized GFP has increased synthesis in mammalian cells, a feature which is advantageous for increasing the signal-to-noise ration when the method relies on fluorescence for detection and sorting. See for instance col. 1, lines 38-45 in Li et al.

22. Claims 1-6, 9, 17-26, 29, 37-43, 51 and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ruley et al in view of Kinzler et al (EP 0 761 822 A2; cited in IDS, Paper #7).

Ruley et al is applied to claims 1-6, 9, 17-19, 21-26, 29, 37-39, 41-43 and 51 as above. Ruley et al does not teach ligating the ends of the cleaved nucleic acid together to form concatamers.

Kinzler et al teach a method of determining the abundance and nature of transcripts corresponding to expressed genes called "serial analysis of gene expression". One aspect of this method is generating tagged gene sequences and concatenating these tagged sequences. See entire document especially Figure 1, p. 3, lines 43-47 and p. 7, lines 23-57. At the time the invention was made it would have been obvious to one of ordinary skill in the art to add the concatenation step of Kinzler et al to the method taught by Ruley et al for sequencing the tagged genes. One of ordinary skill in the art would have been motivated to do so because Kinzler et al teach that their concatenation step allows for efficient analysis in a serial manner, an important time-saving step for any method encompassing large-scale sequencing steps.

Conclusion

Claims 1-52 are rejected.

Certain papers related to this application may be submitted to Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bronwen M. Loeb whose telephone number is (703) 605-1197. The examiner can normally be reached on Monday through Friday, from

10:00 AM to 6:30 PM. A phone message left at this number will be responded to as soon as possible (usually no later than the next business day after receipt by the examiner).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel, can be reached on (703) 305-1998.

Any inquiry of a general nature or relating to the status of this application should be directed to Tracey Johnson, Patent Analyst whose telephone number is (703) 305-2982.

Customer service for Tech Center 1600 may be reached at (703)-308-0198.

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Patent Examiner
Art Unit 1636

October 17, 2002

JAMES KETTER
PRIMARY EXAMINER